

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended). ~~A non-naturally-occurring~~ An isolated nucleic acid comprising a nucleotide sequence ~~that (a) encodes~~ encoding a functional ND4 mitochondrial protein ~~and (b) that differs from a naturally-occurring nucleic acid that encodes a ND4 mitochondrial protein by~~ wherein said sequence comprises at least one codon substitution of a mitochondrial codon with a nuclear codon.

2. (Canceled).

3. (Currently amended). The ~~non-naturally-occurring~~ isolated nucleic acid of claim 1, wherein the codon substitution is UGA to UGG.

4. (Currently amended). The ~~non-naturally-occurring~~ isolated nucleic acid of claim 1, wherein the codon substitution is AGA or AGG to UAA, UAG, or UGA.

5. (Currently amended). The ~~non-naturally-occurring~~ isolated nucleic acid of claim 1, wherein the codon substitution is AUA or AUU to AUG, CUG, or GUG.

6. (Currently amended). The ~~non-naturally-occurring~~ isolated nucleic acid of claim 1, wherein all UGA codons are substituted with UGG codons; all AGA and AGG codons are substituted with UAA, UAG, or UGA codons; and all AUA and AUU codons are substituted with AUG, CUG, or GUG codons.

7. (Currently amended). The ~~non-naturally-occurring~~ isolated nucleic acid of claim 1, wherein the nucleotide sequence comprises the sequence of SEQ ID NO:1.

8. (Currently amended). The ~~non-naturally-occurring~~ isolated nucleic acid of claim 1, wherein the ~~non-naturally-occurring~~ nucleic acid is comprised within an expression vector.

9. (Currently amended). The isolated nucleic acid of claim 8, wherein the expression vector is a plasmid.

10. (Currently amended). The ~~non-naturally-occurring~~ isolated nucleic acid of claim 1, wherein the ~~non-naturally-occurring~~ nucleic acid is comprised within an rAAV virion.

11. (Currently amended). The ~~non-naturally-occurring~~ isolated nucleic acid of claim 1, wherein the non-naturally occurring nucleic acid further comprises a nucleotide sequence encoding a mitochondrial targeting sequence.

12. (Currently amended). The ~~non-naturally-occurring~~ isolated nucleic acid of claim 1, wherein the ~~non-naturally-occurring~~ nucleic acid further comprises a promoter operably linked to the nucleotide sequence.

13. (Currently amended). The ~~non-naturally-occurring~~ isolated nucleic acid of claim 1, wherein the ~~non-naturally-occurring~~ nucleic acid further comprises an enhancer element.

14. (Currently amended). The ~~non-naturally-occurring~~ isolated nucleic acid of claim 1, wherein the non-naturally occurring nucleic acid further comprises a polyA tail.

15. (Currently amended). A cell into which has been introduced a ~~non-naturally-occurring~~ nucleic acid comprising a nucleotide sequence that (a) ~~encodes~~ encodes a functional ND4 mitochondrial protein and (b) ~~that differs from a naturally-occurring nucleic acid that encodes a ND4 mitochondrial protein by~~ wherein said sequence comprises at least one codon substitution of a mitochondrial codon with a nuclear codon.

16. (Original). The cell of claim 15, wherein the cell is a human cell.
17. (Original). The cell of claim 16, wherein the cell is a human nerve cell.
18. (Original). The cell of claim 17, wherein the human nerve cell is located in the optic nerve of a human subject.
19. (Withdrawn). A method for reducing dysfunction in a cell caused by a mtDNA mutation associated with Leber Hereditary Optic Neuropathy, the method comprising the steps of:
- (a) providing a cell having a gene comprising the mtDNA mutation; and
 - (b) introducing into the cell a sufficient amount of a non-naturally occurring nucleic acid comprising (i) a nucleotide sequence that encodes a functional ND4 mitochondrial protein and that differs from a naturally occurring nucleic acid that encodes a ND4 mitochondrial protein by at least one codon substitution and (ii) a nucleotide sequence that encodes a mitochondrial targeting sequence.
20. (Withdrawn). The method of claim 19, wherein the non-naturally occurring nucleic acid further comprises a promoter operably linked to the nucleotide sequence that encodes a functional ND4 mitochondrial protein.
21. (Withdrawn). The method of claim 19, wherein the non-naturally occurring nucleic acid further comprises an enhancer element.
22. (Withdrawn). The method of claim 19, wherein the non-naturally occurring nucleic acid further comprises a polyA tail.
23. (Withdrawn). The method of claim 19, wherein the cell is a human cell.

24. (Withdrawn). The method of claim 23, wherein the cell is a human nerve cell.

25. (Withdrawn). The method of claim 24, wherein the human nerve cell is located in the optic nerve of a human subject.